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Validation of the Treatment Satisfaction Questionnaire for Medication in patients with cystic fibrosis☆

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Abstract

Background: Our objective was to confirm the measurement properties of the Treatment Satisfaction Questionnaire with Medication (TQSM) in patients with cystic fibrosis (CF) receiving inhaled antibiotics.
Methods: The TSQM was included in the EAGER study, a clinical trial comparing a nebulized and a dry powder device for inhaled tobramycin in a CF population with chronic *Pseudomonas aeruginosa* (*Pa*) lung infection, aged 6 years and above ($N=553$). Reliability and validity of the questionnaire were investigated using Cronbach's α and multitrait–multimethod approach.
Results: The TSQM demonstrated very good reliability and construct validity: all Cronbach's α were above 0.86 and all items met the convergent and discriminant validity criteria. In multivariate regressions, higher patient satisfaction and lower perceived impact of side-effects were associated with better treatment compliance.
Conclusions: The TSQM showed very good measurement properties that strongly support its use to assess satisfaction of patients with CF taking inhaled antibiotics.

Keywords: Cystic fibrosis; Tobramycin; Patient satisfaction; Patient compliance; Questionnaires

1. Introduction

Pseudomonas aeruginosa (*Pa*) is the most common respiratory pathogen found in adult patients with CF and is associated with deterioration of lung function, frequent hospitalization and increased risk of mortality [3–5]. Tobramycin inhalation solution is currently recommended for the management of *Pa* infection in CF patients older than 6 years [6,7].

The treatment for CF is complex, burdensome and time-consuming requiring a range of inhaled and systemic medication, physiotherapy and exercise [8,9]. Treatment of *Pa* infection with nebulized antibiotics contributes to this complexity, because of the length of time involved in set-up, administration, cleaning and disinfection. This can lead to issues in terms of patient compliance and persistence. A new drug-device combination, tobramycin inhalation powder (TIP) hard capsules delivered via the T-326 dry powder inhaler, was developed to reduce the time needed to administer the antibiotic and to increase the convenience of the tobramycin inhalation.

Given its importance in high burden diseases and treatments, treatment convenience should be evaluated using a scientifically sound approach and measured with appropriate instruments. Convenience is frequently considered in the wider framework of treatment satisfaction: Patient satisfaction theoretical models state that satisfaction relates to the experience of patients (perceived efficacy, side-effects, and convenience) [10–12] and therefore convenience assessment is commonly part of the assessment of

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treatment satisfaction. In addition, these theoretical models also link patient satisfaction to patient compliance.

Treatment satisfaction has been studied in a number of different conditions involving various modes of administration and devices (e.g. eye drops in glaucoma [13] or self-injection in rheumatoid arthritis [14]). Satisfaction with inhaled therapy has also been investigated in diseases like asthma [15–18], COPD [19] and diabetes [20,21]. While the importance of patient-reported outcomes in CF, in particular health-related quality of life, has been clearly demonstrated [22], satisfaction with inhaled therapy has not yet been carefully studied in CF and no measurement instrument has been investigated in this context.

Our goal was to demonstrate that the Treatment Satisfaction Questionnaire for Medication (TQSM), a widely used generic measure of satisfaction with medication, is a valid and reliable measure of satisfaction in patients with CF and chronic *Pa* lung infection treated with inhaled antibiotics. A second objective was to test in the context of CF the hypotheses about the relationships between satisfaction, convenience and compliance derived from patient satisfaction theoretical models, namely: patient satisfaction is associated to patients' perceived efficacy, side-effects and convenience; patients who are more satisfied have better compliance.

2. Materials and methods

2.1. EAGER study design

This article presents *post-hoc* analyses of data from the "Establish A new Gold standard Efficacy and safety with tobramycin in cystic fibRosis" (EAGER) study conducted from February 2006 to March 2009. The EAGER study was a randomized, open-label, active-controlled, parallel-arm clinical trial in subjects with CF aged 6 years or older where the primary objective was to evaluate the safety of a twice-daily dosing regimen of TIP delivered by the T-326 Inhaler as compared to Tobramyin Inhalation Solution (TIS) delivered with the PARI LC PLUS™ Jet Nebulizer and DeVilbiss PulmoAide™ compressor or an equivalent alternative. Treatment was administered for 28 days followed by 28 days off therapy (1 cycle) for 3 cycles over 24 weeks.

In total, 553 CF patients were randomized to TIP or TIS at a 3:2 ratio. To be eligible, patients had to be older than 6 years; have forced expiratory volume in one second (FEV_1) between 25% and 75% predicted based on Knudson equations [23]; and have sputum or throat cultures positive for *Pa* within 6 months of screening.

The study endpoints were safety assessments (including collection of adverse events and serious adverse events) and efficacy assessments (such as relative change in FEV_1% predicted from baseline and treatment satisfaction). The key safety and efficacy results of the EAGER trial have been reported elsewhere [24].

The EAGER study was approved by an Institutional Review Board or Independent Ethics Committee for each center and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from each patient.

2.2. Treatment Satisfaction Questionnaire for Medication (TSQM)

The TSQM version 1 is a 14-item questionnaire designed as a general measure of treatment satisfaction with medication [10,25]. Its development involved a literature review about treatment satisfaction and qualitative research with patients with chronic illnesses. It was originally validated in a sample of patients with a variety of chronic conditions (arthritis, asthma, major depression, type I diabetes, high cholesterol, hypertension, migraine and psoriasis). The TSQM items are answered on 5- or 7-point Likert type scale and cover four domains, corresponding to distinct aspects related to the satisfaction of patients with their treatment (Effectiveness; Side effects; Convenience and Global satisfaction). A score can be obtained for each domain by summing of the corresponding items transformed on a 0–100 scale; higher values indicate higher satisfaction, better perceived effectiveness, lower burden associated to side-effects, better convenience. Of note, patients who declare experiencing no side-effect automatically have the highest possible side-effect score (i.e. 100).

A sentence was added to the instructions of the TSQM included in the EAGER study to specify that the term "medication", used throughout the questionnaire, should be considered as the combination of the medication and the delivery device. The actual original questions of the TSQM were not altered.

3. Statistical analyses

All randomized patients who received at least one dose of study drug and for whom TSQM data were available for at least one visit were included in analyses, which were performed with the pooled data from the two treatment arms. All analyses were performed using SAS software for Windows version 9.2 (SAS Institute, Cary, NC, USA).

Frequency of missing data and floor and ceiling effects of TSQM scores (i.e. percentages of patients with respectively the lowest and highest possible scores) were tabulated.

Construct validity was evaluated using multitrait–multimethod approach. This approach is based on the correlations between items and scores [26]. The correlation of an item with its own domain should be higher than 0.40 (item convergent validity) and higher than its correlation with all other domains (item discriminant validity). The correlation coefficients between the scores were also investigated.

Reliability coefficients were estimated using Cronbach's coefficient alpha, which assesses internal consistency reliability. Reliability coefficients greater than 0.70 were considered acceptable [27].

Differential item functioning (DIF) between respondents who were assisted by a relative (patients 12 years of age or less) and those who responded on their own was also investigated. Patients who are equally satisfied should give, on average, the same answer to items assessing satisfaction, regardless of the assistance given completing the questionnaire. If this is not the case for an item, then it is said to be functioning differentially [28]. DIF was sought by using logistic regression, a standard DIF detection

technique [29]. As recommended [29], two criteria were jointly considered to characterize DIF, one based on the significance testing of logistic regression parameters (p-value <0.01) and the second based on an estimation of the extent of the difference between the two groups (effect sizes (ES) should be ≥ 0.035).

The relative impact of the three TSQM treatment-specific aspects (Effectiveness, Side effects, and Convenience) on global satisfaction was investigated by applying structural equation modeling (SEM) to the TSQM data. SEM is a statistical method allowing unobserved variables to be studied using the correlations of observed variables [30]. The quality of the hypothesized models can be evaluated using goodness-of-fit indices, with associated thresholds for good fit: root mean square error of approximation (RMSEA) <0.05 (<0.08 for reasonable fit); normed fit index (NFI) >0.90; root mean residuals (RMR) <0.05; comparative fit index (CFI) >0.90.

The relationships between TSQM scores and compliance over cycles 2 and 3 were studied using linear regressions to explain the percentage of doses taken and logistic regressions to explain the compliance status (complier: $\geq 80\%$ doses taken; non-complier: $<80\%$ doses taken), both using the TSQM scores at the assessment preceding the cycle as explanatory variables. For both approaches, multivariate models were obtained using a stepwise selection procedure.

4. Results

4.1. Description of the population

Among the 553 patients randomized in the EAGER trial, 517 received at least one dose of study drug. Of these 517, 460 had available TSQM data for at least one visit; 454 had TSQM data available at the end of the first treatment cycle (week 5); 411 at the end of the second treatment cycle (week 13) and 383 at the end of the third treatment cycle (week 21).

Mean age of the patients of the analysis population was 25.6 years (Table 1). Most of the patients were male (56.2%) and Caucasian (90.1%). Patient compliance was very high (more than 90% of doses were taken over the 3 cycles), although it decreased slightly over the course of the trial (93.4% of patients had taken more than 80% of doses over cycle 1 vs. 86.4% over cycle 3).

Among the 517 patients who received at least one dose of study medication, 217 (42.0%) had a screening FEV_1% predicted between 25% and 50% and 300 (58.0%) between 50% and 75%. Further details on the disease severity of patients included in the EAGER trial can be found elsewhere [24].

Table 1
Description of study population ($N=454$).

	Analysis sample ($N=454$)
Age	
N	454
Mean (SD)	25.6 (10.8)
Children (<13 years)	42 (9.3%)
Adolescent (13–18 years)	78 (17.2%)
Gender	
Male	255 (56.2%)
Race	
Asian	4 (0.9%)
Black	4 (0.9%)
Caucasian	409 (90.1%)
Hispanic	34 (7.5%)
Other	3 (0.7%)
Country	
United States of America	290 (63.9%)
Canada	4 (0.9%)
Italy	32 (7.1%)
Germany	29 (6.4%)
France	18 (4.0%)
Spain	11 (2.4%)
Netherlands	3 (0.7%)
Greece	2 (0.4%)
Switzerland	1 (0.2%)
United Kingdom	10 (2.2%)
Israel	15 (3.3%)
Australia	23 (5.1%)
Mexico	8 (1.8%)
Chile	4 (0.9%)
Colombia	4 (0.9%)
FEV_1 at baseline (Predicted %)	
N	452
Mean (SD)	52.8 (14.5)
Compliance over cycle 1	
N	451
Mean percentage of doses taken (SD)	96.5 (10.0)
Compliant patients ($\geq 80\%$ doses taken)	424 (93.4%)
Compliance over cycle 2	
N	405
Mean percentage of doses taken (SD)	93.9 (15.0)
Compliant patients ($\geq 80\%$ doses taken)	362 (88.1%)
Compliance over cycle 3	
N	379
Mean percentage of doses taken (SD)	93.6 (14.5)
Compliant patients ($\geq 80\%$ doses taken)	331 (86.4%)

SD: Standard deviation; FEV_1: Forced expiratory volume in one second.

4.2. Psychometric properties of the TSQM

4.2.1. Quality of completion and distribution of scores

The psychometric properties of the TSQM were explored using data from the TSQM assessment at week 5. They were replicated at week 13 and 21, showing very similar results (data not shown). At week 5, 95% patients completed all TSQM items. The item with the most missing data was item 9 ("Treatment ease of use"), which was missing for 6 (1.3%) patients (Table 2).

None of the TSQM scores had a floor effect (Table 3). The Side effects score showed a strong ceiling effect, with 72% of the patients having the highest possible score (cases when patients declare having no side-effects); the Convenience and Global satisfaction scores had a mild ceiling effect (with 15% and 13% of patients at the maximum score of 100, respectively).

4.2.2. Construct validity

All items met the item convergent and divergent validity criteria (Table 3). The pattern of correlations between the TSQM scores was in line with reasonable assumptions: Global satisfaction was well correlated with the 3 treatment-specific

Table 2
TSQM items: missing data; differential item functioning (DIF) results (week 5, $N=545$).

Items	Missing data [a] N (%)	Uniform DIF	
		p-value	ES
Q1. Satisfaction with prevention/treatment	2 (0.4)	0.6141	0.0006
Q2. Satisfaction with symptom relief	2 (0.4)	0.3283	0.0005
Q3. Satisfaction with time to start working	2 (0.4)	0.1752	0.0011
Q4. Side-effect presence	0 (0.0)	–	–
Q5. Bother from side-effects	0 (0.0)	0.7191	0.0000
Q6. Side-effects interference with physical function	1 (0.7)	0.4215	0.0000
Q7. Side-effects interference with mental function	1 (0.7)	0.9621	0.0073
Q8. Impact of side-effects on satisfaction	1 (0.7)	0.0160	0.0004
Q9. Treatment easy to use	6 (1.3)	0.5533	0.0012
Q10. Easy planning of use	0 (0.0)	0.1433	0.0000
Q11. Intake convenience	0 (0.0)	0.6280	0.0001
Q12. Confidence in benefits	3 (0.7)	0.0107	0.0000
Q13. Balance between good and bad things	2 (0.4)	0.4800	0.0026
Q14. Global satisfaction	0 (0.0)	0.7068	0.0015

ES: Effect Size.
[a] Q5,Q6,Q7 and Q8 are dependent on Q4 response. Frequencies and percentages are calculated according to patients who answered Yes at Q4: 138 at week 5, 111 at week 13 and 92 at week 21.

aspects (0.73 with Effectiveness, 0.43 with Convenience, 0.43 with Side-effects); the correlations between these 3 specific dimensions (which assess fairly independent aspects) were lower, ranging from 0.20 to 0.43.

4.2.3. Internal consistency

The internal consistency reliability of the TSQM scores was very good, with Cronbach's alpha ranging from 0.86 for Global satisfaction to 0.88 for Convenience (Table 3).

4.3. Impact of completion mode

Patients who were assisted when completing the TSQM had statistically significantly higher Convenience ($p=0.016$) and Effectiveness ($p<0.001$) scores than patients who completed the questionnaire on their own (Table 3). Global satisfaction and Side effects scores were also higher for patients who were assisted when completing the questionnaire than for patients who answered on their own, but the differences were not statistically significant.

In the DIF detection phase, neither the mode of completion nor the interaction between mode of completion and TSQM score showed a statistically significant effect on any item responses and all ES were lower than the predefined threshold of 0.035 (Table 2). Therefore, no item was functioning differentially between patients who were assisted and those who were not.

4.4. Exploratory model of treatment satisfaction

A model was prespecified to explore how patient satisfaction with inhaled antibiotics was formed according to patient satisfaction theoretical models (Fig. 1): it assumed that the three treatment-specific TSQM domains (Effectiveness, Convenience; Side effects) affected Global satisfaction. Overall, the fit of this model to the week 5 data was good, with most of the indices meeting the predefined criteria (RMSEA=0.09; NFI=0.93; CFI=0.95; GFI=0.92; AGFI=0.87; standardized RMR=0.06).

Effectiveness showed a strong contribution to Global satisfaction (standardized estimate linking Effectiveness to Global satisfaction of 0.69). Side effects and Convenience had weaker, but non-negligible, impacts on Global satisfaction (with respective standardized estimates of 0.17 and 0.21). Similar results were obtained using TSQM data collected at week 13 and 21 (data not shown).

4.5. Relationship between TSQM scores and compliance

At week 5, all TSQM scores had a significant relationship with compliance over the subsequent on-treatment period (cycle 2=between week 9 and 13) in the univariate linear regression models (Table 4). Only the Side effects and Convenience scores were significantly related to compliance in the multivariate models. These results were very similar for satisfaction at week 13 and compliance over cycle 3 (between week 17 and 21).

In the logistic models (when satisfaction was considered dichotomously, above or below 80% doses taken), compliance was related to the Side effects and Global satisfaction scores at week 5 and to Side effects, Effectiveness and Global satisfaction scores at week 13. In the multivariate models, Side effects and Global satisfaction (only at week 13) were significantly associated with compliance status.

5. Discussion

The purpose of this analysis was to investigate satisfaction with inhaled antibiotics in patients with CF and chronic *Pa* infection, with a focus on two main questions: is it appropriate to use the TSQM to measure satisfaction with inhaled antibiotics in patients with CF and *Pa* lung infection; what treatment-related aspects are key in the formation of patient satisfaction in this context and to what extent is this satisfaction likely to impact patient compliance?

The analyses performed on the EAGER study data supported the good psychometric properties of the TSQM in patients with CF and chronic *Pa* infection treated by inhaled tobramycin. The quality of completion of the fourteen TSQM items was almost perfect with very few missing answers, the four-domain structure of the questionnaire was confirmed and the four scores shown to be reliable. Unfortunately, the extremely small samples from most of the countries of the study prevented the cross-cultural validity of the TSQM to be investigated.

Cystic fibrosis commonly affects young patients who may have difficulties completing on their own a questionnaire about treatment satisfaction. In the EAGER study, younger patients were therefore assisted when filling the TSQM and we investigated whether such assistance impacts the assessment. A consistent shift in the distribution of all TSQM scores towards better satisfaction was observed in patients who were assisted when completing the questionnaire but none of the

Table 3
TSQM scores: distribution and psychometric properties at week 5 (N=454).

Score	N	Mean score (SD)			N (%) at floor	N (%) at ceiling	Range of item-scale correlations	Convergent validity criterion [a](% of items)	Discriminant validity criterion [b](% of items)	Cronbach's alpha
		All patients	Patients who completed the TSQM alone (N=412)	Patients who were assisted when completing the TSQM (N=42)						
Effectiveness	453	70.2 (18.4)	69.2 (18.3)	79.7 (16.9)	1 (0.22)	34 (7.51)	0.64–0.81	100.0	100.0	0.87
Side effects	453	92.3 (15.7)	91.9 (16.2)	96.1 (10.0)	0 (0.00)	325 (71.74)	0.51–0.83	100.0	100.0	0.87
Convenience	454	72.2 (21.2)	71.4 (21.3)	79.6 (18.9)	1 (0.22)	67 (14.76)	0.75–0.80	100.0	100.0	0.88
Global satisfaction	454	73.0 (19.8)	72.4 (20.0)	78.8 (16.1)	1 (0.22)	60 (13.22)	0.72–0.78	100.0	100.0	0.86

[a] Convergent validity criterion met if item-scale correlation greater than 0.4.
[b] Discriminant validity criterion met if the correlation of an item with its own scale is greater than the correlation of this item with all the other scales.

fourteen TSQM items showed DIF, indicating that the differences in score could not be related to a response bias in any specific TSQM item. The score differences might be due to a systematic bias consistently affecting all items, such as social desirability (the often unconscious desire to give a positive image to others by giving responses that correspond to socially admitted opinions [31]). These differences may also be the sign of a difference in the concepts measured in the context of different completion mode (it is actually likely that the satisfaction measured in children is a combination of the parent and child perspective). Nonetheless, the absence of systematic difference in TSQM item response, and the small number of children relative to the total sample clearly support the results obtained on the overall sample. However, it is critical to note that our results do not warrant the use of the TSQM to assess specifically treatment satisfaction in children. The TSQM was not designed, nor validated in this context of use. Further research on this topic (both qualitative and quantitative) is needed to get a better understanding of the question of the assessment of treatment satisfaction of children with CF and identify (or develop) an instrument to be used in this purpose.

While the TSQM demonstrated good psychometric properties in the context of the EAGER study, it would be relevant to consider assessing satisfaction with inhalers using a measurement instrument specifically designed for this purpose (as has been done for example in asthma treatment [15]). There may be specific aspects of CF patients' experience with their inhaled treatment that are of importance to them but not captured by the TSQM. Further research on this question is needed to warrant a proper and comprehensive assessment of satisfaction with the device in the framework of CF inhaled antibiotic therapy.

Also, the assessment of satisfaction in this study was only in the context of treatment of *Pa* infection with inhaled tobramycin. It could be worthwhile to investigate satisfaction with other inhaled treatments in CF. While it is likely that these study results could be directly generalized to other inhaled antibiotics, the other inhaled therapies (bronchodilators, mucus mobilizers, anti-inflammatory therapies) have specific features and are used in different contexts, so they would probably deserve specific investigations. It might be relevant to scrutinize whether using the TSQM is appropriate in these various contexts.

Our results showed that the most important driver of satisfaction with inhaled tobramycin was perceived effectiveness of the treatment. However, perceived side effects and convenience appeared to play a non-negligible role in the formation of satisfaction. This contribution of convenience to patients' satisfaction confirmed how relevant satisfaction is when considering delivery devices, for which convenience is a key feature.

A key reason for studying patient satisfaction is that, according to theoretical models, satisfaction should affect patient behavior [10,11,32]. Therefore patient satisfaction with a treatment is expected to be linked to patient compliance. In our analyses, a significant association between TSQM scores and compliance was indeed found, even though the size of the association was not large. In particular, patients' global satisfaction was markedly related to compliance. Interestingly,

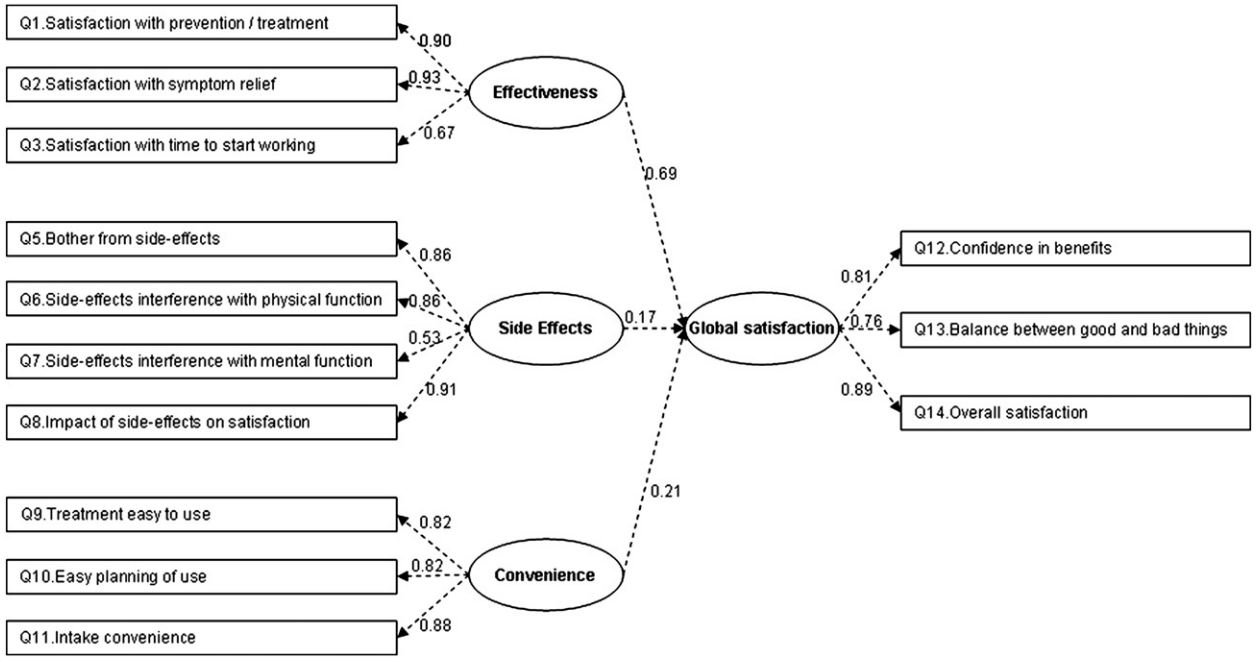

Fig. 1. Hypothesized TSQM domain measurement models and impact of the three TSQM treatment-specific aspects (Effectiveness, Side effects, and Convenience) on global satisfaction — results from Structural Equation Modeling (week 5, $N=545$).This figure summarizes the results of the structural equation model about the link between treatment satisfaction and patient experience with their treatment (Perceived efficacy, side-effects and convenience). This graphical representation combines the specification of how each unobserved variable is measured by the items of the questionnaire and the relationships between the unobserved variables. Ovoids represent unobserved variables; rectangles represent observed variables (items) measuring these unobserved variables; dotted arrows represent the hypothesized links between the variables; parameters relative to each arrow are standardized parameters (that represent the strength of the association between the linked variables).

the side effect score showed a consistent association with compliance, independently of global satisfaction. This indicates the importance of the perceived impact of side effects as a key driver of patients' behavior regarding their inhaled treatment. Specifically, among TSQM scores, perceived impact of side effects was the main factor explaining the fact that some patients took less than 80% of doses over a cycle. This could indicate that, even if global satisfaction affects compliance, it is predominantly the perceived side effects that actually lead to non-compliance.

However, these results should be considered cautiously as they were obtained from clinical trial data. The clinical trial setting imposes conditions that certainly affect compliance. Patients are selected and aware of being part of a clinical study and rigorous monitoring is put in place; this naturally translates to very high levels of compliance (between 93% and 96% of doses were taken, depending on the cycle considered). Thus, the behaviors observed in the EAGER trial do not reflect patient behavior in real life. The limited magnitude of the association between satisfaction and compliance may be due to this constraining clinical trial context and global satisfaction may in fact have a greater effect on actual compliance in real life. However, this possibility can only be confirmed within an observational real-life study. In addition, the

Table 4
Linear and logistic regression results explaining compliance using TSQM scores.

		Linear regression [a]				Logistic regression [b]			
		Univariate		Multivariate (after stepwise selection)		Univariate		Multivariate (after stepwise selection)	
	Parameter	Estimate	*p*-value	Estimate	*p*-value	Estimate	*p*-value	Estimate	*p*-value
Effect of satisfaction assessed at week 5 on the compliance over cycle 2	Effectiveness	**0.09**	**0.0305**	–	–	0.01	0.3005	–	–
	Side effects	**0.18**	**0.0007**	**0.14**	**0.0137**	**0.03**	**0.0023**	**0.03**	**0.0025**
	Convenience	**0.07**	**0.0531**	–	–	0.01	0.0559	–	–
	Global satisfaction	**0.14**	**0.0011**	**0.10**	**0.0215**	**0.02**	**0.0291**	–	–
Effect of satisfaction assessed at week 13 on the compliance over cycle 3	Effectiveness	**0.14**	**0.0009**	–	–	**0.02**	**0.0141**	–	–
	Side effects	**0.27**	**<.0001**	**0.20**	**0.0010**	**0.04**	**<.0001**	**0.03**	**0.0057**
	Convenience	**0.08**	**0.0146**	–	–	0.01	0.0826	–	–
	Global satisfaction	**0.18**	**<.0001**	**0.13**	**0.0021**	**0.03**	**0.0008**	**0.02**	**0.0464**

In bold, significant estimates at the threshold of 20% for univariate regressions, and at the threshold of 5% for multivariate regressions.

[a] Linear regression with percentage of doses taken over the cycle as explained variable.

[b] Logistic regression with dichotomized compliance (≥80% doses taken vs. <80% doses taken) as explained variable.

analyses of compliance used the threshold of 80% of dose taken to separate good compliance from poor compliance. While it is a widely used threshold [33,34], it is not supported by any scientific rationale in the context of CF and further research about the definition of good compliance to CF treatment is therefore needed to support this approach.

In conclusion, the TSQM showed good measurement properties that strongly support the use of this instrument to assess patient satisfaction with inhaled CF antibiotic treatments. In addition, despite the restrictive features related to the clinical trial setting, an association between patient satisfaction and compliance was shown: higher patient satisfaction and lower perceived impact of side effects were found to be associated with better compliance with CF inhaled treatment.

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Conflict of interest

Antoine Regnault is an employee of MAPI Consultancy, a consulting company commissioned by Novartis for this study. Maria-Magdalena Balp and Karoly Kulich are employees of Novartis. Muriel Viala-Danten was an employee of MAPI Consultancy at the time of the study.

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Laurent Estève programmed the statistical analyses.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jcf.2012.04.007.

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